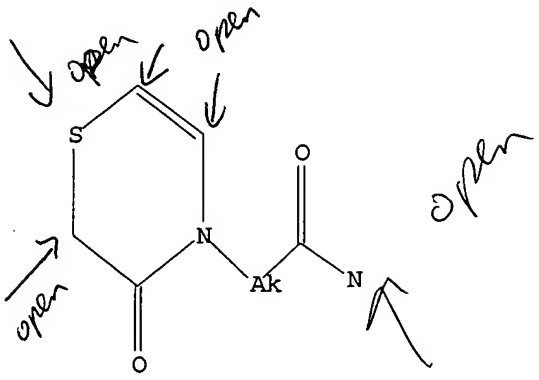
Broad search



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 12:22:41 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   2137 TO ITERATE

 46.8% PROCESSED    1000 ITERATIONS                                1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        39968 TO    45512
PROJECTED ANSWERS:               1 TO      129

L2             1 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 12:22:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  44051 TO ITERATE

100.0% PROCESSED   44051 ITERATIONS                              16 ANSWERS
SEARCH TIME: 00.00.01

L3            16 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             155.42     155.63

FILE 'CAPLUS' ENTERED AT 12:22:57 ON 14 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```

FILE COVERS 1907 - 14 Dec 2004 VOL 141 ISS 25
FILE LAST UPDATED: 13 Dec 2004 (20041213/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 2 L3

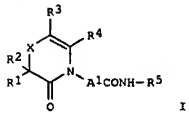
=> d ibib abs hitstr tot

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:78369 CAPLUS
DOCUMENT NUMBER: 134:131554
TITLE: Preparation of novel thiazine or pyrazine derivatives as chymase inhibitors
INVENTOR(S): Matsumoto, Junzo; Nishimura, Kazuo; Ban, Masakazu; Fujimura, Ken-ichi; Kobayashi, Naoyuki; Hori, Masanori; Honda, Takahiro
PATENT ASSIGNEE(S): Santen Pharmaceutical Co., Ltd., Japan; Matsumoto, Eiko
SOURCE: PCT Int. Appl., 278 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007419	A1	20010201	WO 2000-JP4964	20000726
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2380218	AA	20010201	CA 2000-2380218	20000726
JP 2001097957	A2	20010410	JP 2000-224667	20000726
EP 1211249	A1	20020605	EP 2000-949890	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6713472	B1	20040330	US 2002-31540	20020118
US 2004097496	A1	20040520	US 2003-713891	20031113
PRIORITY APPLN. INFO.:			JP 1999-210907	A 19990726
			WO 2000-JP4964	W 20000726
			US 2002-31540	A3 20020118

OTHER SOURCE(S): MARPAT 134:131554
GI

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

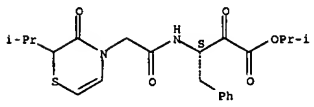


I

AB Novel compds. having as the main skeleton 3-oxo-3,4-dihydro-2H-1,4-thiazine or 2-oxo-1,2,3,4-tetrahydropyrazine, which are represented by general formula [I; wherein X = S, R6-(A2)n-N; R1, R2 = H, lower alkyl, cycloalkyl, cycloalkyl, aryl; R3, R4 = H, lower alkyl, cycloalkyl, aryl, heteroaryl; R5 = H, lower alkyl, cycloalkyl, aryl, A3-A4-R7; wherein R6 = H, lower alkyl, cycloalkyl, HO, lower alkoxy, aryl, aryloxy, heteroaryl; R7 = H, lower alkyl, HO, lower alkoxy, aryl, aryloxy, NH2, lower alkylamino, arylamino, aromatic or nonarom. heterocyclyl; n = 0,1; A1 = lower alkylene; A2 = CO, SO2; A3 = lower alkylene; A4 = CO, oxalyl; the above lower alkyl is optionally substituted by halo, HO, lower alkoxy, aryl, or aryloxy; the above lower alkoxy or lower alkylene is optionally substituted by aryl], are prepared These compds. are useful for the treatment of chymase-related diseases such as myocardial infarction, heart failure, vascular restenosis after PTCA, hypertension, diabetes complications, allergies, and asthma. (3S)-3-[[[[(3R)-4-benzoyl-3-isopropyl-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrazin-1-yl]methyl]carbonyl]amino]-2-oxo-4-phenylbutanoic acid iso-Pr ester which showed IC50 of 0.20 + 10-6 M against chymase.
IT 322396-01-0P 322396-02-1P 322396-03-2P
322396-04-3P 322396-05-4P 322396-07-6P
322396-08-7P 322396-90-7P 322396-91-8P
322396-92-9P 322396-93-0P 322396-94-1P
322396-95-2P 322396-96-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel thiazine or pyrazine derivs. as chymase inhibitors for treatment of chymase-related diseases)
RN 322396-01-0 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

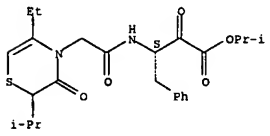
Absolute stereochemistry.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



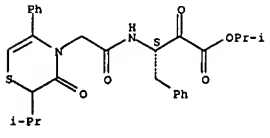
RN 322396-02-1 CAPLUS
CN Benzenebutanoic acid, β-[[[5-ethyl-2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322396-03-2 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-2-(1-methylethyl)-3-oxo-5-phenyl-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

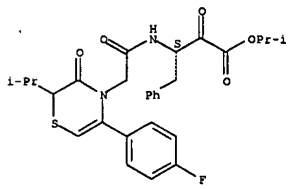
Absolute stereochemistry.



RN 322396-04-3 CAPLUS
CN Benzenebutanoic acid, β-[[[5-(4-fluorophenyl)-2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

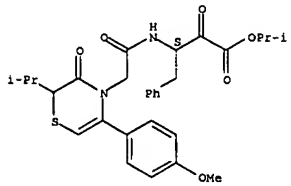
Absolute stereochemistry.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



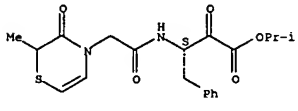
RN 322396-05-4 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-5-(4-methoxyphenyl)-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



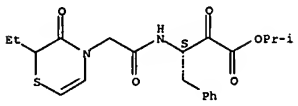
RN 322396-07-6 CAPLUS
CN Benzenebutanoic acid, β-[[(2,3-dihydro-2-methyl-3-oxo-4H-1,4-thiazin-4-yl)acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



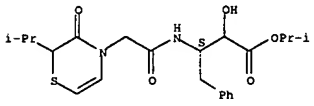
RN 322396-08-7 CAPLUS
CN Benzenebutanoic acid, β-[[(2-ethyl-2,3-dihydro-3-oxo-4H-1,4-thiazin-4-yl)acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.



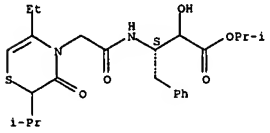
RN 322396-90-7 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322396-91-8 CAPLUS
CN Benzenebutanoic acid, β-[[[5-ethyl-2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



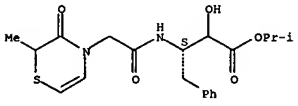
RN 322396-92-9 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-2-(1-methylethyl)-3-oxo-5-phenyl-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

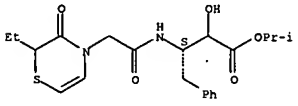
RN 322396-95-2 CAPLUS
CN Benzenebutanoic acid, β-[[(2,3-dihydro-2-methyl-3-oxo-4H-1,4-thiazin-4-yl)acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322396-96-3 CAPLUS
CN Benzenebutanoic acid, β-[[(2-ethyl-2,3-dihydro-3-oxo-4H-1,4-thiazin-4-yl)acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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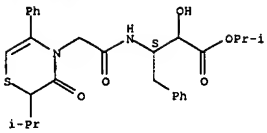
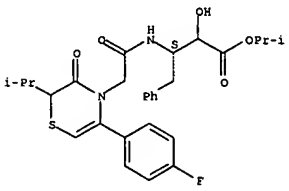
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



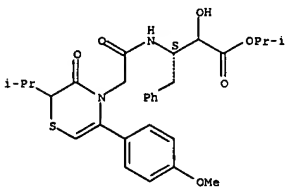
RN 322396-93-0 CAPLUS
CN Benzenebutanoic acid, β-[[[5-(4-fluorophenyl)-2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322396-94-1 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-5-(4-methoxyphenyl)-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:954579 CAPLUS
DOCUMENT NUMBER: 123:340166
TITLE: Preparation of novel 2-benzylidenethiazine or 2-benzylidenethiomorpholine derivatives for treatment of cataracts
INVENTOR(S): Kawashima, Yoichi; Ota, Atsutoshi; Mibu, Hiroyuki
PATENT ASSIGNEE(S): Santen Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 666261	A1	19950809	EP 1995-101413	19950202
EP 666261	B1	19970507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07258238	A2	19951009	JP 1995-8710	19950124
JP 2964382	B2	19991018		
US 5556841	A	19960917	US 1995-378502	19950126
CN 1112924	A	19951206	CN 1995-102904	19950129
NO 9500387	A	19950807	NO 1995-387	19950202
AT 152714	E	19970515	AT 1995-101413	19950202
CA 2141780	AA	19950805	CA 1995-2141780	19950203
FI 9500493	A	19950805	FI 1995-493	19950203
PRIORITY APPLN. INFO.:			JP 1994-12979 A	19940204

OTHER SOURCE(S): MARPAT 123:340166
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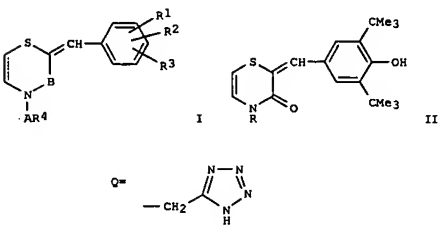
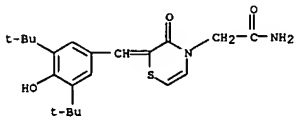


AB The title compound [I; R1 = (un)protected OH; R2 = lower alkyl: R3 = H, lower alkyl, (un)protected HO, lower alkoxy, and the said lower alkyl can be substituted by hydroxy, which can be protected by a hydroxy protective group, amino or lower alkylamino; R4 = CO2H which can be converted into

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ester or amide, tetrazolyl, phosphono which can be converted into ester or
amide, sulfonyl which can be converted into ester or amide; A = alkylene; B = CO, CS or CH2; the dotted line represents a single bond or double bond) are prepd. These compds. I have protein stabilizing effect and suppress lipid peroxide formation. Thus, lithiation of 1,4-thiazine with (Me2CH)2NLi in THF at -70° followed by addn. to 3,5-di-tert-butyl-4-hydroxybenzaldehyde at -70°, mesylation with mesyl chloride in the presence of Et3N in CH2Cl2 and elimination reaction gave 50% 2-benzylidene-1,4-thiazin-3-one deriv. (II; R = H). Alkylation of the latter compd. with bromoacetonitrile in the presence of NaH in THF gave II (R = CH2CN) which underwent cycloaddn. reaction with NaN3 in the presence of NH4Cl in DMF at 110° to give II (R = Q) (III). III at 10-4 M inhibited 99.5% the heat coagulation of bovine serum albumin in DMSO-0.2 M potassium phosphate buffer at 67° for 2 min. It in vitro suppressed 100% the lipid peroxide formation in microsomes of rat liver in the presence of Fe2+ and ascorbic acid in 0.04 M Tris buffer contg. 0.09 M KCl.

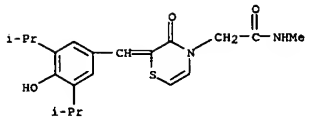
IT **170919-86-5P 170919-87-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzylidenethiazine or -thiomorpholine derivs. as protein stabilizers and lipid peroxide formation inhibitors for treatment of cataracts)

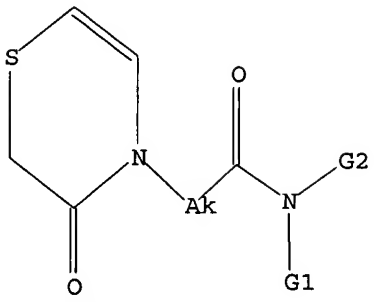
RN 170919-86-5 CAPLUS
CN 4H-1,4-Thiazine-4-acetamide, 2-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methylene]-2,3-dihydro-3-oxo- (9CI) (CA INDEX NAME)



RN 170919-87-6 CAPLUS
CN 4H-1,4-Thiazine-4-acetamide, 2,3-dihydro-2-[[4-hydroxy-3,5-bis(1-methylethyl)phenyl]methylene]-N-methyl-3-oxo- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)





G1 H,Me

G2 H,Ak,Cb,CH2,CH

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 08:21:04 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   2137 TO ITERATE

 46.8% PROCESSED    1000 ITERATIONS                                 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        39968 TO    45512
PROJECTED ANSWERS:               1 TO      129

L2             1 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 08:21:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  44051 TO ITERATE

100.0% PROCESSED   44051 ITERATIONS                               16 ANSWERS
SEARCH TIME: 00.00.01

L3            16 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               155.42     155.63

FILE 'CAPLUS' ENTERED AT 08:21:17 ON 14 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 14 Dec 2004 VOL 141 ISS 25
FILE LAST UPDATED: 13 Dec 2004 (20041213/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 2 L3

=> d ibib abs hitstr tot

own work

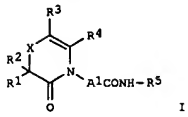
L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:78369 CAPLUS
DOCUMENT NUMBER: 134:131554
TITLE: Preparation of novel thiazine or pyrazine derivatives as chymase inhibitors
INVENTOR(S): Matsumoto, Junzo; Nishimura, Kazuo; Ban, Masakazu; Fujimura, Ken-ichi; Kobayashi, Naoyuki; Hori, Masanori; Honda, Takahiro
PATENT ASSIGNEE(S): Santen Pharmaceutical Co., Ltd., Japan; Matsumoto, Eiko
SOURCE: PCT Int. Appl., 278 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007419	A1	20010201	WO 2000-JP4964	20000726
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2380218	AA	20010201	CA 2000-2380218	20000726
JP 2001097957	A2	20010410	JP 2000-224667	20000726
EP 1211249	A1	20020605	EP 2000-949890	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6713472	B1	20040330	US 2002-31540	20020118
US 2004097496	A1	20040520	US 2003-713891	20031113
PRIORITY APPLN. INFO.:			JP 1999-210907	A 19990726
			WO 2000-JP4964	W 20000726
			US 2002-31540	A3 20020118

OTHER SOURCE(S): MARPAT 134:131554
GI

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

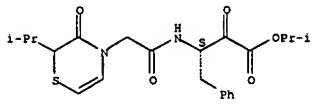
AB Novel compds. having as the main skeleton 3-oxo-3,4-dihydro-2H-1,4-thiazine or 2-oxo-1,2,3,4-tetrahydropyrazine, which are represented by general formula [I; wherein X = S, R6-(A2)n-N; R1, R2 = H, lower alkyl, cycloalkyl, cycloalkyl, aryl; R3, R4 = H, lower alkyl, cycloalkyl, aryl, heteroaryl; R5 = H, lower alkyl, cycloalkyl, aryl, A3-A4-R7; wherein R6 = H, lower alkyl, cycloalkyl, HO, lower alkoxy, aryl, aryloxy, heteroaryl; R7 = H, lower alkyl, HO, lower alkoxy, aryl, aryloxy, NH2, lower alkylamino, arylamino, aromatic or nonarom. heterocyclyl; n = 0,1; A1 = lower alkylene; A2 = CO, SO2; A3 = lower alkylene; A4 = CO, oxalyl; the above lower alkyl is optionally substituted by halo, HO, lower alkoxy, aryl, or aryloxy; the above lower alkoxy or lower alkylene is optionally substituted by aryl], are prepared These compds. are useful for the treatment of chymase-related diseases such as myocardial infarction, heart failure, vascular restenosis after PTCA, hypertension, diabetes complications, allergies, and asthma. (3S)-3-[[[[(3R)-4-benzoyl-3-isopropyl-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrazin-1-yl]methyl]carbonyl]amino]-2-oxo-4-phenylbutanoic acid iso-Pr ester which showed IC50 of 0.20 + 10-6 M against chymase.

IT **322396-01-0P 322396-02-1P 322396-03-2P**
322396-04-3P 322396-05-4P 322396-07-6P
322396-08-7P 322396-90-7P 322396-91-8P
322396-92-9P 322396-93-0P 322396-94-1P
322396-95-2P 322396-96-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel thiazine or pyrazine derivs. as chymase inhibitors for treatment of chymase-related diseases)

RN 322396-01-0 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

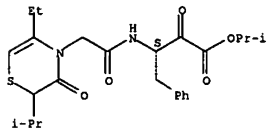
Absolute stereochemistry.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



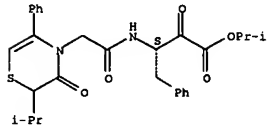
RN 322396-02-1 CAPLUS
CN Benzenebutanoic acid, β-[[[5-ethyl-2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322396-03-2 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-2-(1-methylethyl)-3-oxo-5-phenyl-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

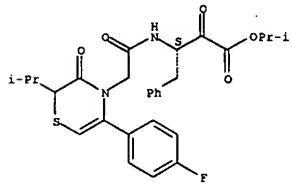
Absolute stereochemistry.



RN 322396-04-3 CAPLUS
CN Benzenebutanoic acid, β-[[[5-(4-fluorophenyl)-2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

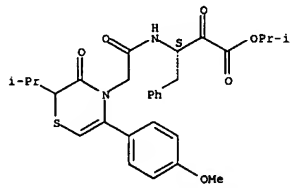
Absolute stereochemistry.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



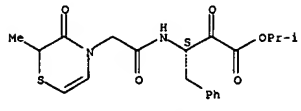
RN 322396-05-4 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-5-(4-methoxyphenyl)-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



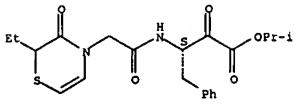
RN 322396-07-6 CAPLUS
CN Benzenebutanoic acid, β-[[(2,3-dihydro-2-methyl-3-oxo-4H-1,4-thiazin-4-yl)acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



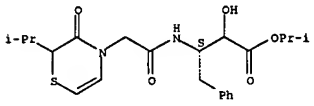
RN 322396-08-7 CAPLUS
CN Benzenebutanoic acid, β-[[(2-ethyl-2,3-dihydro-3-oxo-4H-1,4-thiazin-4-yl)acetyl]amino]-α-oxo-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.



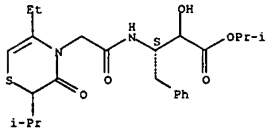
RN 322396-90-7 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322396-91-8 CAPLUS
CN Benzenebutanoic acid, β-[[[5-ethyl-2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



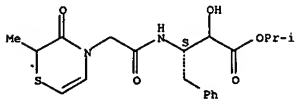
RN 322396-92-9 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-2-(1-methylethyl)-3-oxo-5-phenyl-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

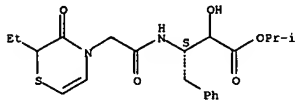
RN 322396-95-2 CAPLUS
CN Benzenebutanoic acid, β-[[(2,3-dihydro-2-methyl-3-oxo-4H-1,4-thiazin-4-yl)acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



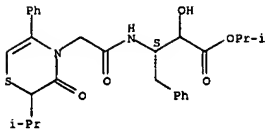
RN 322396-96-3 CAPLUS
CN Benzenebutanoic acid, β-[[(2-ethyl-2,3-dihydro-3-oxo-4H-1,4-thiazin-4-yl)acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



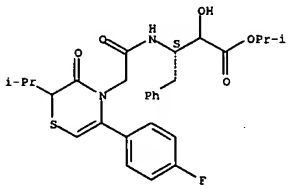
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



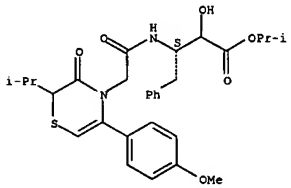
RN 322396-93-0 CAPLUS
CN Benzenebutanoic acid, β-[[[5-(4-fluorophenyl)-2,3-dihydro-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322396-94-1 CAPLUS
CN Benzenebutanoic acid, β-[[[2,3-dihydro-5-(4-methoxyphenyl)-2-(1-methylethyl)-3-oxo-4H-1,4-thiazin-4-yl]acetyl]amino]-α-hydroxy-, 1-methylethyl ester, (βS)- (9CI) (CA INDEX NAME)

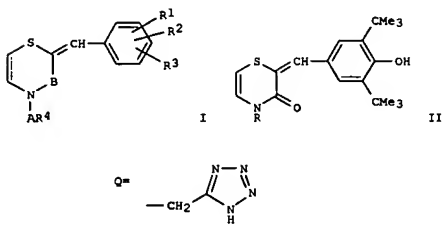
Absolute stereochemistry.



L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:954579 CAPLUS
DOCUMENT NUMBER: 123:340166
TITLE: Preparation of novel 2-benzylidenethiazine or 2-benzylidenethiomorpholine derivatives for treatment of cataracts
INVENTOR(S): Kawashima, Yoichi; Ota, Atsutoshi; Mibu, Hiroyuki
PATENT ASSIGNEE(S): Santen Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 666261	A1	19950809	EP 1995-101413	19950202
EP 666261	B1	19970507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07258238	A2	19951009	JP 1995-8710	19950124
JP 2964382	B2	19991018		
US 5556841	A	19960917	US 1995-378502	19950126
CN 1112924	A	19951206	CN 1995-102904	19950129
NO 9500387	A	19950807	NO 1995-387	19950202
AT 152714	E	19970515	AT 1995-101413	19950202
CA 2141780	AA	19950805	CA 1995-2141780	19950203
FI 9500493	A	19950805	FI 1995-493	19950203
PRIORITY APPLN. INFO.:			JP 1994-12979 A	19940204

OTHER SOURCE(S): MARPAT 123:340166
GI

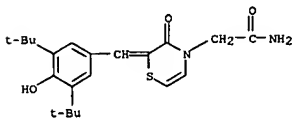


AB The title compound [I; R1 = (un)protected OH; R2 = lower alkyl: R3 = H, lower alkyl, (un)protected HO, lower alkoxy, and the said lower alkyl can be substituted by hydroxy, which can be protected by a hydroxy protective group, amino or lower alkylamino; R4 = CO2H which can be converted into

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ester or amide, tetrazolyl, phosphono which can be converted into ester or
amide, sulfonyl which can be converted into ester or amide; A = alkylene; B = CO, CS or CH2; the dotted line represents a single bond or double bond] are prepd. These compds. I have protein stabilizing effect and suppress lipid peroxide formation. Thus, lithiation of 1,4-thiazine with (Me2CH)2NLi in THF at -70° followed by addn. to 3,5-di-tert-butyl-4-hydroxybenzaldehyde at -70°, mesylation with mesyl chloride in the presence of Et3N in CH2Cl2 and elimination reaction gave 50% 2-benzylidene-1,4-thiazin-3-one deriv. (II; R = H). Alkylation of the latter compd. with bromoacetonitrile in the presence of NaH in THF gave II (R = CH2CN) which underwent cycloaddn. reaction with NaN3 in the presence of NH4Cl in DMF at 110° to give II (R = Q) (III). III at 10-4 M inhibited 99.5% the heat coagulation of bovine serum albumin in DMSO-0.2 M potassium phosphate buffer at 67° for 2 min. It in vitro suppressed 100% the lipid peroxide formation in microsomes of rat liver in the presence of Fe2+ and ascorbic acid in 0.04 M Tris buffer contg. 0.09 M KCl.

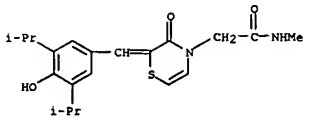
IT **170919-86-5P 170919-87-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzylidenethiazine or -thiomorpholine derivs. as protein stabilizers and lipid peroxide formation inhibitors for treatment of cataracts)

RN 170919-86-5 CAPLUS
CN 4H-1,4-Thiazine-4-acetamide, 2-[[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]methylene]-2,3-dihydro-3-oxo- (9CI) (CA INDEX NAME)



RN 170919-87-6 CAPLUS
CN 4H-1,4-Thiazine-4-acetamide, 2,3-dihydro-2-[[4-hydroxy-3,5-bis(1-methylethyl)phenyl]methylene]-N-methyl-3-oxo- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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L4	2688	544/58.2, 514/227.5, 514/227.8, 540/544, 540/575, 540/598	USPAT	OR	OFF	2004/12/14 12:17
L5	346	chymase$	USPAT	OR	OFF	2004/12/14 12:17
L6	6	l4 and l5	USPAT	OR	OFF	2004/12/14 12:17

KH

Day : Tuesday
Date: 12/14/2004

Time: 12:19:35

PALM INTRANET

Inventor Information for 10/713891

Inventor Name	City	State/Country
NISHIMURA, KAZUO	OSAKA-SHI	JAPAN
BAN, MASAKAZU	OSAKA-SHI	JAPAN
FUJIMURA, KEN-ICHI	OSAKA-SHI	JAPAN
KOBAYASHI, NAOYUKI	OSAKA-SHI	JAPAN
HORI, MASANORI	OSAKA-SHI	JAPAN
HONDA, TAKAHIRO	OSAKA-SHI	JAPAN
MATSUMOTO, JUNZO	ASHIYA-SHI	JAPAN
MATSUMOTO, EIKO	ASHIYA-SHI	JAPAN

Appln Info | Contents | Petition Info | Atty/Agent Info | Continuity Data | Foreign Data

Search Another: Application# [ ] Search **or Patent#** [ ] Search

PCT / [ ] / [ ] Search **or PG PUBS #** [ ] Search

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1: Nippon Yakurigaku Zasshi. 1999 Oct;114 Suppl 1:41P-47P. Related Articles, Li

[Pathophysiological roles of chymase and effects of chymase inhibitor]

[Article in Japanese]

Takai S, Jin D, Miyazaki M.

Department of Pharmacology, Osaka Medical College, Japan.

Human chymase forms angiotenin (ANG) I to ANG II, whereas the roles of ANG II generated by chymase and the effects of chymase inhibitors have bee unclear. On the other hand, rat chymase could not convert ANG I to ANG II. isolated rat arteries, the ANG I-induced vascular contraction was completely suppressed by angiotensin-converting enzyme (ACE) inhibitor only. Howeve 30% of ANG I-induced vascular contraction in isolated human arteries was suppressed by an ACE inhibitor, but the remainder was blocked by chymostatin. In hamster hypertensive models, ANG II formation by ACE, bu not by chymase, in vascular tissues plays an important role in maintaining hypertension. ANG II formation also induces vascular remodeling such as neointima formation. After balloon injury of vessels in dog, chymase and AC activities were significantly increased in the injured vessels. In this model, ar ANG II receptor antagonist was effective in preventing neointimal formation after balloon injury of vessels in dog, but an ACE inhibitor was ineffective. I dog grafted veins, the activities of chymase and ACEmin the grafted vein we significantly increased 15- and 2-fold, respectively, compared with those in t symmetrical veins. The intimal area of the grafted vein was reduced by a chymase inhibitor. Therefore, chymase-dependent ANG II formation plays a important role in the proliferative response, and chymase inhibitors may appe useful for preventing vascular proliferation.

Publication Types:
- Review

PMID: 10629853 [PubMed - indexed for MEDLINE]

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